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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROARK, JESSICA H	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,671	TJELLSTROM ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/5/03, is acknowledged.
   Claims added: 13-14.
   Claims currently amended: 1, 4, 9 and 10.
   Claims pending: 1-14.

Claims 11-12 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the Paper filed 3/14/03.

Claims 1-10 and 13-14 *are under consideration in the instant application.*

2. This Office Action will be in response to applicant's arguments, filed 9/5/03.
   The rejections of record can be found in the previous Office Action.

   It is noted that New Grounds of Rejection are set forth herein.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 120 is again acknowledged.

Applicant's arguments in the response filed 9/5/03 that an immunoglobulin preparation prepared by pooling immunoglobulin from human volunteers (e.g., provisional application 60/074,193 at page 10 line 20 to page 11 at line 7; instant disclosure at page 7, lines 13-23) must necessarily be polyclonal are found convincing. It is noted that the instant disclosure is a continuation-in-part of parent application USSN 09/247,396 and discloses this inherent property (e.g., page 6 at lines 22-27). It is appropriate to accord benefit of an earlier filing date for subject matter inherently supported by, but not actually disclosed in, a parent application to a continuation-in-part application now disclosing the inherent subject matter. *In re Davies and Hopkins*, 177 USPQ 381 (CCPA 1973).

Accordingly, the effective filing date of the instant claims is considered to be that of provisional application 60/074,193, i.e., 2/10/1998.

Claim Rejections – 35 U.S.C. §§ 102 and 103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
   A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. As previously noted regarding Tjellstrom et al. (Acta Paediatr 1997; 86:221-223, of record) the statement by the publisher provided in parent application USSN 09/247,396 that Tjellstrom et al. was not mailed until, at the earliest, Feb 11, 1997 has been made of record in the instant file. As noted supra, the effective filing date of the instant claims is 2/10/98. Further, although Tjellstrom et al. was filed within 1 year of Applicant's earliest effective filing date, it is not 'by another".

6. The previous rejection of claims 1, 3-7 and 9-10 under 35 U.S.C. 102(b) as being anticipated by Tjellstrom et al. (Acta Paediatr 1997; 86:221-223, IDS) as evidenced by Eibl and Wolf (in "Therapeutic Immunology", eds Austen et al., 1996 Blackwell Sciences, Inc., Cambridge, Massachusetts, Chapter 22 "Immunoglobulin A", pages 297-310, of record) is withdrawn for the reasons set forth supra.

7. The claims as amended on 9/5/03 encompass in their breadth any human immunoglobulin preparation. Although Applicant's species election is again acknowledged, the following rejection is set forth with respect to the breadth of the amended claims.

8. Claims 1-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Salfeld et al. (U.S. Pat. No. 6,509,015).

Salfeld et al. teach human antibodies to human TNFα and the application of these fully human antibodies to methods which benefit from the reduction of TNF activity (see entire document, e.g. Abstract). An antibody is another name for an immunoglobulin (see e.g., column 7 at lines 17-53).

Salfeld et al. teach that the human antibodies of the invention may be administered orally to treat TNF-mediated diseases (columns 21-22, especially column 22 at lines 19-32). Salfeld et al. also teach that the route and mode of administration depends upon the desired results (column 22 at lines 1-18).

Salfeld et al. teach that the art recognized that antibodies to TNF could be used to treat intestinal disorders, including inflammatory bowel disease in general and ulcerative colitis and Crohn's disease in particular (column 27 at lines 16-29). Inflammatory bowel disease is inherently a form of mucosal inflammation.

Salfeld et al. also teach that the human antibodies can be of the IgG isotype, and disclose a working example that is an IgG4 human antibody (columns 9-10, see especially Table). A composition comprising one of these monoclonal antibodies would

Formulation of the immunoglobulin in a pharmaceutically acceptable carrier is taught at columns 21-22, including enteric coatings for oral administration (column 22 at lines 19-32).

Salfeld et al. teach that the dosage of antibody administered is to be optimized to achieve the desired therapeutic result (see columns 22-23), but that in general, the dosage will be in the range of 0.1 to 20 mg/kg (column 23 at lines 27-38). For an average 70 kg adult, this corresponds to a dose of 0.007g to 1.4g.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the human antibody used in the methods as taught be Salfeld et al.

The reference teachings thus anticipate the instant claimed invention.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-10 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hassig (U.S. Pat. No. 4,676,982, of record) and Hardie (U.S. Pat. No. 4,477,432, IDS).

Applicant's arguments, filed 9/5/03 have been fully considered but have not been found convincing. Applicant's arguments are addressed below.

The claims as amended are drawn to a method of treating inflammatory bowel disease, including ulcerative colitis and Crohn's disease, by orally administering to a patient a human immunoglobulin preparation comprising at least about 25% IgG, including wherein the immunoglobulin preparation is pooled polyclonal immunoglobulin.

As previously noted, Hassig teaches and claims a method of treating chronic inflammatory diseases of the bowel, including ulcerative colitis and Crohn's disease, by intravenously administering an effective dose of polyvalent immunoglobulin (see entire document, e.g., Abstract and claims).

Hassig teaches that the immunoglobulin preparation is intact IgG obtained from blood serum fractions (i.e., is a pooled human polyclonal immunoglobulin preparation, see column 1, especially lines 32-48).

An IgG preparation is necessarily at least about 25% IgG polyclonal antibodies.

Hassig differs from the instant method by not teaching oral administration and the doses and formulations for oral administration.

However, Hardie teaches that immunoglobulin preparations prepared for intravenous administration could also be administered orally without a loss of therapeutic efficacy (see entire document).

Hardie teaches that oral administration of Ig, including IgG, has advantages over parenteral (including intravenous) administration because oral administration avoided the pain of an injection, by provided an easy means of administering the composition, and provided an administration route by which larger doses could be administered if needed (see column 2, especially "Summary of the Invention").

Hardie teaches formulating the oral immunoglobulin preparation as part of a pharmaceutically acceptable carrier, and teaches encapsulation of the composition, which would provide an enteric coating (see columns 3-4.

Hardie teaches that the formulation administered in the examples of the invention for treatment of enteric infection contained 14 mg/dl (1.4 mg/mL) of IgG and that 1-8 mL/kg/day was administered (1.4-11.2 mg/kg). Thus for an adult of 70 kg, the corresponding dose would be 98-784 mg, which falls within dosage recited in instant claim 7.

The Examiner has previously argued that the ordinary artisan at the time the invention was made would have found it obvious to administer the IgG preparation taught by Hassig for the treatment of inflammatory bowel disease by the oral route, using pharmaceutically acceptable carriers appropriate for oral administration. Both Crohn's disease and ulcerative colitis are examples of inflammatory bowel disease involving mucosal inflammation. The ordinary artisan would have been motivated to substitute oral administration for intravenous administration because Hardie teaches that oral administration is advantageous compared to parenteral, including intravenous, administration. Finally, given the teachings of Hardie that orally administered immunoglobulin preparations, including IgG preparations, could be administered orally without loss of function for the treatment of other enteric diseases, the ordinary artisan at the time the invention was made would have had a reasonable expectation that oral administration would also be effective in the methods taught by Hassig.

Applicant argues that because Hardie focuses on treatment of enteric infections, rather than inflammatory disease and Hassig does not address the oral administration of immunoglobulins as taught by Hardie, the ordinary artisan would not have been motivated to combine the references absent the instant disclosure.

However, as noted supra Hardie teaches that oral administration of immunoglobulin for intestinal infections was not only possible, but advantageous. While Hardie's teaching focus on the application of oral immunoglobulin therapy for infection, that does not mean that the ordinary artisan armed with the teachings of Hassig would not have appreciated that the method could advantageously be applied to the methods of treating inflammatory bowel disease taught by Hassig. In addition, while the Examiner has clearly acknowledged that Hardie does not teach treatment of inflammatory bowel disease since the rejection was made under 35 USC 103(a), not 35 USC 102, specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See *CTS Corp. v. Electro Materials Corp. of America* 202 USPQ 22 (DC SNY); and *In re Burckel* 201 USPQ 67 (CCPA).

The amendment to the claims to broaden the scope of the method to encompass any human immunoglobulin preparation does not affect the rejection of record.

Therefore, the Examiner maintains that the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. For the reasons set forth supra, Applicant has established that Tjellstrom et al. is not available as prior art reference against the instant claims.

Therefore, the previous rejection of claims 1- 8 under 35 U.S.C. 103(a) as being unpatentable over Tjellstrom et al. (Acta Paediatr 1997; 86:221-223, IDS) as evidenced by Eibl and Wolf (in "Therapeutic Immunology", eds Austen et al., 1996 Blackwell Sciences, Inc., Cambridge, Massachusetts, Chapter 22 "Immunoglobulin A", pages 297-310, of record) and the instant disclosure on page 10 at lines 29-31 stating that IgAbulin is an appropriate commercial immunoglobulin preparation for use in the instant methods; in view of Hassig (U.S. Pat. No. 4,676,982, of record) is withdrawn.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
November 19, 2003

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11/19/03